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THE UNIVERSITY OF ROCHESTER
COLLEGE OF ARTS AND SCIENCE
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DEPARTMENT OF CHEMISTRY

October 30, 1975

Professor Francis H. C. Crick
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Dear Francis:

Many thanks for your recent letter which has done wonders to clarify my own confusion about handedness in superhelical DNA structures. The stiff rubber tubing experiment you described is really beautiful in that it demonstrates how a left-handed toroidal helix (the state of DNA in SV-40 when bound to histones) is converted to a right-handed interwound helix when histones have been removed. In the absence of histones, the latter structure has lower free energy than the former structure and therefore arises spontaneously. It is therefore the form readily prepared in the laboratory.

I now agree that intercalative drugs and dyes act to unwind both types of superhelical structures! This being the case...the left-handed toroidal structure would tend to kink, a process which would tend to unwind this left-handed helix. So....kinking would thermodynamically be favored to exist in chromatin.

Now, with regard to Vinograd's estimate of the number of superhelical turns per nu body. All of Jerry's work is done with the right-handed interwound helix.... and the question in my own mind is: Are the number of superhelices in this structure necessarily the same as in the original left-handed toroidal structure? I think this would depend on how "stiff" DNA is and the size (compactness) of the left-handed toroidal turns. This is again easily demonstrated by the stiff rubber tubing experiment. If one makes very tight left-handed toroidal superhelical turns, joins the ends and releases the superhelices ....one gets about the same number of right-handed superhelices formed in the interwound structure. If, however, one makes larger diameter left-handed toroidal superhelical turns (these possess lower potential energy) and does this experiment, one gets considerably fewer right-handed superhelices in the interwound structure. Thus, Vinograd's estimate (1.2 superhelical turns per nu body), when translated into left-handed toroidal turns may be a serious underestimate of the true state of affairs. Do you agree with this?

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With this in mind, I have done a few calculations using the kinking scheme I showed you....where a kink involves the formation of a v-type notch in the narrow groove of DNA.

Our estimates for the kink angle are currently about 45°. Let us assume that kinks occur every ten base-pairs and that 170 base-pairs are intimately associated with the four histones in each nu body. This means 16 kinks and (16 x 45°) about 2 left-handed (kinked) toroidal turns per nu body. The diameter of such an object is about 90 Å .... so we can envision these turns winding around the outside of the histone core.

Now, 2 kinked left-handed toroidal turns are equivalent to about 1.5 unkinked left-handed toroidal turns (this assumes that associated with each kink is an unwinding of about 11-12°). 1.5 unkinked left-handed toroidal turns may give rise to 1.2 unkinked right-handed interwound turns per nu body.

What do you think of this?

Best regards.

Sincerely,
Henry
Henry M. Sobell

P.S. We have recently solved a 4:4 crystalline complex between 9-aminoacridine and iodoCpG. The structure consists of two 2:2 complexes, each of which look much like the ethidium structures. 9-Aminoacridine therefore intercalates into these miniature double-helical structures!

With regards Jerry's comment about handedness... I suggest we forget it. His comment was a quick one between changing planes in Russia.... and I (or he) may have misunderstood the question about handedness.